

c.) Remarks

Claim 3, 11, 13, 14, 17, 19-21, 26, 28, 29, 32 and 34 have been amended for better idiomatic format and grammatical usage. Claims 1 and 5 have been cancelled to reduce the issues and new Claims 35-41 are presented in order to more specifically recite various preferred embodiments of the present invention. No new matter has been added.

Claims 1, 2, 5, 10, 13-15, 17 and 20 are rejected under 35 U.S.C. §102(b) as anticipated by WO99/36555 or EP870841. Claims 1, 2, 5, 9-17 and 20 are rejected under 35 U.S.C. §103(a) as being obvious over WO99/36555 in combination with EP870841. Claims 3 and 24-32 are rejected as obvious over WO99/09180 taken with EP870841.

This rejection is respectfully traversed. However, prior to setting forth their bases for traversal, Applicants would like to briefly discuss the salient features of the present invention and *inter alia*, its patentable nature over the prior art.

The present invention, as recited in claim 2, relates to a process for producing GDP-glucose using a GTP precursor as a substrate and, as an enzyme source, a culture broth of a microorganism capable of forming GTP from the GTP precursor, or a treated product of the culture broth. New claim 35 relates to the equivalent process for producing GDP-fucose.<sup>1/</sup>

WO 99/36555 teaches enzymatically producing GDP-fucose using GDP-mannose (substrate) with GDP-mannose dehydratase (*gmd*) and YEF B (corresponding to *wcaG*). *Gmd* and YEF B are extracted from disrupted recombinant *E. coli* capable of expressing those enzymes.

In the Office Action (page 3, lines 19-21), the Examiner asserts that such enzymes can be interpreted to fall within the phrase "a concentrated product of a culture

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<sup>1/</sup> Accordingly, in claim 35, an enzyme source capable of forming GTP from a GTP precursor is not required.

broth" as the term is utilized in the claims. However, as explained below, such is not the case.

The plain English usage distinguishes the reference; a "concentrated product" is just that, a product obtained from concentrating the whole culture broth. That differs in kind from the *extract* of the culture broth taught by the prior art. In that regard, as the Examiner contends, if the extract of WO 99/36555 was "a concentrated product of a culture broth", NADPH would not be required to produce GDP-fucose. In contrast, NADPH is an essential component to produce GDP-fucose in WO 99/36555 (item 7 at page 52 and claim 17, etc.). However, since the present invention concentrates the entire culture broth, added NADPH is not required.

That is, since the present invention does not use an enzyme (whether crude extract or purified) alone, the present invention supplies the coenzyme required for the enzyme reactions. Therefore, the present efficiently produces GDP-fucose without added NADPH (see Example 5).

Accordingly, it is apparent that WO 99/3655 teaches enzymes *per se* and does not teach Applicants' "concentrated product of a culture broth".

EP 870 841 discloses producing GDP-fucose directly from a saccharide without forming and accumulating GKDM using, as enzyme sources, culture broths of a microorganism capable of producing GKDM from GTP and a saccharide, and of a microorganism capable of producing GDP-fucose from GKDM. EP 870 841 is at least plainly more relevant than WO 99/365555, in that EP 870 841 does not teach culture broth extracts. However, EP 870 841 does not teach or suggest processes that form and accumulate GKDM. That is, the process of the present invention necessarily forms and accumulates GKDM without feedback inhibition by GDP-fucose to *gmd* by (i) forming GKDM from a saccharide and GTP and (ii) then converting accumulated GKDM into

GDP-fucose.<sup>2/</sup> Such is not taught by EP 870 841.

Accordingly, the prior art does not make out a *prima facie* case of anticipation. Nor, for that matter, is the subject matter of the present invention rendered obvious by the prior art.

Furthermore, WO 99/09180 shows (see, e.g., example 11) producing GKDM using GDP-mannose as a substrate with an enzyme extract prepared from recombinant *E. coli*. However, WO 99/09180 also does not disclose or suggest using culture broths or preparations as enzyme sources.

Moreover, even if, arguendo, a *prima facie* case of obviousness is made out by taking any or all of the prior art collectively, such is overcome by the evidence already of record herein.

The present invention produces GDP-fucose in an amount of 14.0 g/l (see page 35, line 10 to page 36, last line, Example 5), whereas EP 870 841<sup>3</sup> produces GDP-fucose only in an amount of 3.7 g/l (see page 37, lines 1-5 of the present specification). This remarkable (nearly four-fold) improvement is plainly useful to those of ordinary skill, but is entirely unexpected in view of the prior art.

Accordingly, any case of obviousness is overcome by the showings of record.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 2, 3, 9-22 and 24-41 are pending, claims 18, 19, 21, 22, 33 and 34 being withdrawn from prosecution with mandatory rejoinder thereof being respectfully

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<sup>2/</sup> See claim 2, line 9.

<sup>3/</sup> EP 870 841 is the closest prior art since WO 99/3655 and WO 99/09180 use extracts of culture broths and not concentrated products of culture broths, which is plainly a salient feature of the present invention.

requested upon allowance of an antecedent claim.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Lawrence S. Perry", is written over a horizontal line.

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## Revised Notice\*

### AMENDMENTS MAY NOW BE SUBMITTED IN REVISED FORMAT

The United States Patent and Trademark Office (USPTO) is permitting applicants to submit amendments in a revised format as set forth below. Further details of this practice are described in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, signed January 31, 2003, expected to be published in *Official Gazette* on February 25, 2003 (Notice posted on the Office's web site at

<http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm>). The revised amendment format is essentially the same as the amendment format that the Office is considering adopting via a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. The Office plans to adopt such a revision to 37 CFR 1.121 by July of 2003 at which point compliance with revised 37 CFR 1.121 will be mandatory.

Effective immediately, all applicants may submit amendments in reply to Office actions using the following format. Participants in the Office's electronic file wrapper prototype<sup>1</sup> receiving earlier notices of the revised practice may also employ the procedures set out below.

### REVISED FORMAT OF AMENDMENTS

#### Begin on separate sheets:

Each section of an Amendment (e.g., Claim Amendments, Specification Amendments, Drawing Amendments, and Remarks) should begin on a separate sheet. *For example*, in an amendment containing a.) introductory comments, b.) amendments to the claims, c.) amendments to the specification, and d.) remarks, each of these sections must begin on a separate sheet. This will facilitate the process of separately indexing and scanning of each part of an amendment document for placement in an electronic file wrapper.

#### Two versions of amended part(s) no longer required:

The current requirement in 37 CFR 1.121(b) and (c) to provide two versions (a clean version and a marked up version) of each replacement paragraph, section or claim will be waived where an amendment is submitted in revised format below. The requirements for substitute specifications under 37 CFR 1.125 will be retained.

#### A) Amendments to the claims:

Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.

- (1) The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number by one of the following: (original), (currently amended), (previously amended), (canceled), (withdrawn), (new), (previously added), (reinstated – formerly claim # ), (previously reinstated), (re-presented – formerly dependent claim # ), or (previously re-presented). The text of all pending claims under examination must be submitted each time any claim is amended. Canceled and withdrawn claims should be indicated by only the claim number and status.
- (2) All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim should be shown by strikethrough (for deleted matter) or underlining (for added matter). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended" will include markings.
- (3) The text of pending claims not being amended must be presented in clean version, i.e., without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version.

<sup>1</sup> The Office's Electronic File Wrapper prototype program is described in *USPTO ANNOUNCES PROTOTYPE OF IMAGE PROCESSING*, 1265 Off. Gaz. Pat. Office 87 (Dec. 17, 2002) ("Prototype Announcement"), and applies only to Art Units 1634, 2827 and 2834.

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- (4) A claim may be canceled by merely providing an instruction to cancel. Listing a claim as canceled will constitute an instruction to cancel. Any claims added by amendment must be indicated as (new) and shall not be underlined.
- (5) All of the claims in each amendment paper must be presented in ascending numerical order. Consecutive canceled or withdrawn claims may be aggregated into one statement (e.g., Claims 1 – 5 (canceled)).

**Example of listing of claims (use of the word "claim" before the claim number is optional):**

Claims 1-5 (canceled)

Claim 6 (withdrawn)

Claim 7 (previously amended): A bucket with a handle.

Claim 8 (currently amended): A bucket with a ~~green~~ blue handle.

Claim 9 (withdrawn)

Claim 10 (original): The bucket of claim 8 with a wooden handle.

Claim 11 (canceled)

Claim 12 (re-presented – formerly dependent claim 11) A black bucket with a wooden handle.

Claim 13 (previously added): A bucket having a circumferential upper lip.

Claim 14 (new): A bucket with plastic sides and bottom.

**B) Amendments to the specification:**

Amendments to the specification must be made by presenting a replacement paragraph or section marked up to show changes made relative to the immediate prior version. An accompanying clean version is not required and should not be presented. If a substitute specification is being submitted to incorporate extensive amendments, both a clean version (which will be entered) and a marked up version must be submitted as per current 37 CFR 1.125.

**C) Amendments to drawing figures:**

Drawing changes must be made by presenting replacement figures which incorporate the desired changes and which comply with § 1.84. An explanation of the changes made must be presented in the remarks section of the amendment. Any replacement drawing sheet must include all of the figures appearing on the immediate prior version of the sheet, even though only one figure may be amended. The figure or figure number of the amended drawing should not be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Any questions regarding the submission of amendments pursuant to the revised practice set forth in this flyer should be directed to the following legal advisors in the Office of Patent Legal Administration (OPLA): Elizabeth Dougherty ([Elizabeth.Dougherty@uspto.gov](mailto:Elizabeth.Dougherty@uspto.gov)), Gena Jones ([Eugenia.Jones@uspto.gov](mailto:Eugenia.Jones@uspto.gov)) or Joe Narcavage ([Joseph.Narcavage@uspto.gov](mailto:Joseph.Narcavage@uspto.gov)). For information on the waiver or legal aspects of the prototype, please contact Jay Lucas ([Jay.Lucas@uspto.gov](mailto:Jay.Lucas@uspto.gov)), Senior Legal Advisor (PGTLA) or Rob Clarke ([Robert.Clarke@uspto.gov](mailto:Robert.Clarke@uspto.gov)), Senior Legal Advisor (OPLA). Alternatively, further information may be obtained by calling OPLA at (703) 305-1616.

\* Revised Notice: See Sec. B) for changes relating to substitute specifications, and Sec. C) for changes on replacement drawing practice.